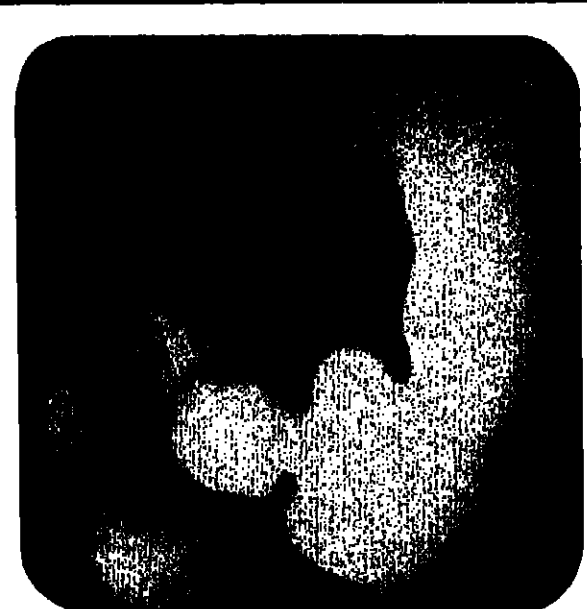


The Upper Functional G.I. Disorder

The Pseudo-ulcer



Ulcer-like symptoms: no G.I. pathology

The patient is convinced it's an ulcer. However, symptoms are not quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient to understand and how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist.* Where milder cases may respond to counsel-

ing alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms. In these cases, Librax as an adjunct can greatly contribute to the course of therapy. Its dual action can offer relief of both painful symptoms and excessive anxiety, because each capsule contains 5 mg chlorthalidone HCl and 2.5 mg cimetidine Br. The antianxiety action of Librax® (chlorthalidone HCl) makes Librax exceptional

An adjunct
in anxiety-related upper
functional G.I. disorders

Librax®

Each capsule contains 5 mg chlorthalidone HCl and 2.5 mg cimetidine Br.

among drugs for certain gastrointestinal disorders associated with excessive anxiety; the cimetidine bromide (Quarzan™) component furnishes dependable antisecretory-antispasmodic action. Dosage is flexible; it may be adjusted according to your patient's requirements within the range of 1 or 2 capsules three or four times daily, up to 8 capsules daily in divided doses.

*Rome HP, Brannick TL: Orientation and mechanism of functional disorders; Clinophysiology correlation, chap. 188, in *Gastroenterology*, edited by Rockus HL. Philadelphia, WB Saunders Company, 1965, p. 1116

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlorthalidone hydrochloride and/or cimetidine bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librax (chlorthalidone hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in

pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlorthalidone hydrochloride is used alone, drows-

iness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EKG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlorthalidone hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other antispasmodics and/or low residue diets.



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A B C D

Medical Tribune

and Medical News

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Behind News: CIR Delegates Discussing Strike Talks



Dr. Jay Dobkin (standing at right in T-shirt), chairman of negotiating committee of Committee of Interns and Residents, reports to C.I.R. delegate caucus on progress of talks during strike affecting 23 New York City hospitals.

New York Strike May Set Pattern For Hospital Staff Work Changes

Medical Tribune Report

NEW YORK—Last month's strike by some 2,100 interns and residents in New York City hospitals didn't last long, but it was watched closely around the country and the terms of the settlement that was reached may serve as precedent for changes in other cities.

Although the strike was a success from the point of view of the young doctors who led and participated in it, interviews conducted by MEDICAL TRIBUNE suggest that strikers and non-strikers alike had mixed feelings about the action.

The strike was called by the Committee of Interns and Residents, representing house officers at city and voluntary health care facilities in the greater New York area, against the League of Voluntary Hospitals, a

group of 11 hospital centers and their municipal affiliates.

At issue were house staff duty schedules—as much as 58 hours at a stretch, with weekly on-duty time often exceeding 100 hours for junior house staff.

Another area of disagreement was so-called "out-of-title" work. In many cases, it was alleged by the C.I.R., interns and residents were forced to do the work of nurses, technicians, aides, and even messengers because of understaffing.

According to the terms of the settlement, no later than July 1, 1976, no house staff officer will be required to perform call duty more than one night in three. Also, by May 1, 1975, standing committees will be set up in each

Continued on page 18

NIH Study Finds Nitroglycerin Beneficial in Acute Infarction

By HARRIET PAGE
Medical Tribune Staff

BETHESDA, MD.—The use of nitroglycerin is proving to be "consistently beneficial" in the treatment of patients with acute myocardial infarction, according to Dr. Stephen E. Epstein, of the Cardiology Branch of the National Heart and Lung Institute.

Twelve patients have so far been treated in a collaborative study headed by Dr. Epstein. And so far, he told MEDICAL TRIBUNE, with a follow-up of up to six months, the clinical response is bearing out the beneficial results he and his associates found in earlier animal studies.

Briton Fears Pool Of Hepatitis B Virus Rising in Newborn

By FRANCES GOODNIGHT
Medical Tribune Staff

NEW YORK—A pool of "chronic carriers" of hepatitis B virus may be building up among children born to women who became infected with it during pregnancy or who are asymptomatic carriers themselves, a British investigator warned here.

Calling the situation a "cause of utmost concern," Dr. Arie J. Zuckerman, of the London School of Hygiene and Tropical Medicine, urged that all pregnant women be screened routinely for hepatitis B surface antigen just as blood donors are tested.

The virologist noted that one in 1,000 healthy volunteer blood donors in Britain are carriers of hepatitis B antigen—one in 500 among certain social groups—and that the carrier incidence reaches 20 per cent in some countries.

The finding of active infection or a carrier state in pregnant women should be the signal to undertake measures to protect the child, Dr. Zuckerman told a symposium on infections of the fetus and newborn presented by the New York University School of Medicine

Continued on page 12

1969-73 Study Results

Control Program Reduces Hospital Infections by 10%

Medical Tribune Report

ROCKFORD, ILL.—What is believed to be the first long-term study to gauge the overall effect of hospital infections on morbidity and mortality, and to show that the rate of such infections can be reduced, was described by Dr. Larry D. Edwards, Associate Professor of Medicine and chief of infectious diseases at Rockford School of Medicine, in a recent interview.

Continued on page 13

making rounds at press time

SELL YOUR KIDNEY? An unemployed Pittsburgh man deeply in debt tried it and had a prospective buyer, until Dr. Keith Hruska, co-director of the Chromalloy American Kidney Center, Washington U., St. Louis, talked them out of it because it probably was not a suitable match. "I can

understand the seller's desperation — and there appears to be an increase lately in attempts to sell organs — but we have to avoid a situation in which the rich can buy their health and the poor cannot," Dr. Hruska told MT. He attributed the increase in sales attempts to the ailing economy. Dr. Ira Grier, medical director of the National Kidney Foundation added that "Buying and selling organs will create a black market, with sales to the highest bidder."

OPPOSED — H.E.W. is "paying close attention," a spokesman told MT to some 2,300 letters opposing Secretary Casper Weinberger's "maximum allowable costs" plan aimed to cut Medicare and Medicaid drug costs. Opposition appears evenly divided the spokesman said, among pharmacists, M.D.s, and industrial and professional societies. M.D.s are chiefly concerned with questions of quality and interchangeability and interference with practice of medicine.

POSTPONED — Medicare-Medicaid utilization review requirements for hospitals and nursing homes are now set back to July 1 because many rural areas were unable to establish procedures for former Feb. 1 deadline.

VINYL CL — New occupational standards that call for maximum exposure of 5 ppm of vinyl chloride are in effect pending appeal by manufacturers, after Supreme Court decision not to stay April 1 effective date for the standards.

Wednesday, April 16, 1975

Expert Panel Backs 'Right to Volunteer' as Research Subject

Medical Tribune Report

WASHINGTON—Should soldiers, prisoners, and the poor be used in medical experiments, and if so, under what conditions?

A panel of legal and medical experts discussed these questions at a forum of the National Academy of Sciences on "Experiments and Research with Humans: Values in Conflict." While the range of opinions expressed was wide, the panelists managed—with one exception—to find some common ground of agreement on principle.

"Prisons are inherently coercive," said Alvin J. Bronstein, Executive Director-Counsel, National Prison Project, American Civil Liberties Union Foundation, "and therefore experimen-

tation on prisoner subjects should not be permitted." Mr. Bronstein's criteria were drawn from the Nuremberg code, which stipulates that medical experiments on humans can only be legally carried out with the subject's "voluntary consent," and such consent can only be given by a person "so situated as to be able to exercise free power of choice." Overt and subtle pressures on prisoners to take part in research experiments disqualifies them from being true volunteers, in Mr. Bronstein's view.

He was the only speaker who would exclude a whole class of people from participating as subjects in experiments—or, in the words of Dr. Albert B. Sabin, Distinguished Research Profes-

sor of Biomedicine, Medical University of South Carolina, "deprive them of the right to volunteer." Dr. Sabin and the other panelists, Dr. William N. Hubbard, Jr., President, the Upjohn Company, and Dr. Jay Katz, Adjunct Professor of Law and Psychiatry, Yale Law School, weighed the social risks and benefits of human experiments, and tried to define standards of "informed consent."

Malaria, Polio Drugs Cited

Dr. Sabin asserted that some of the most important preventive and therapeutic drugs in current use, including those against malaria and polio, could not have been developed without research on volunteers in the uniquely

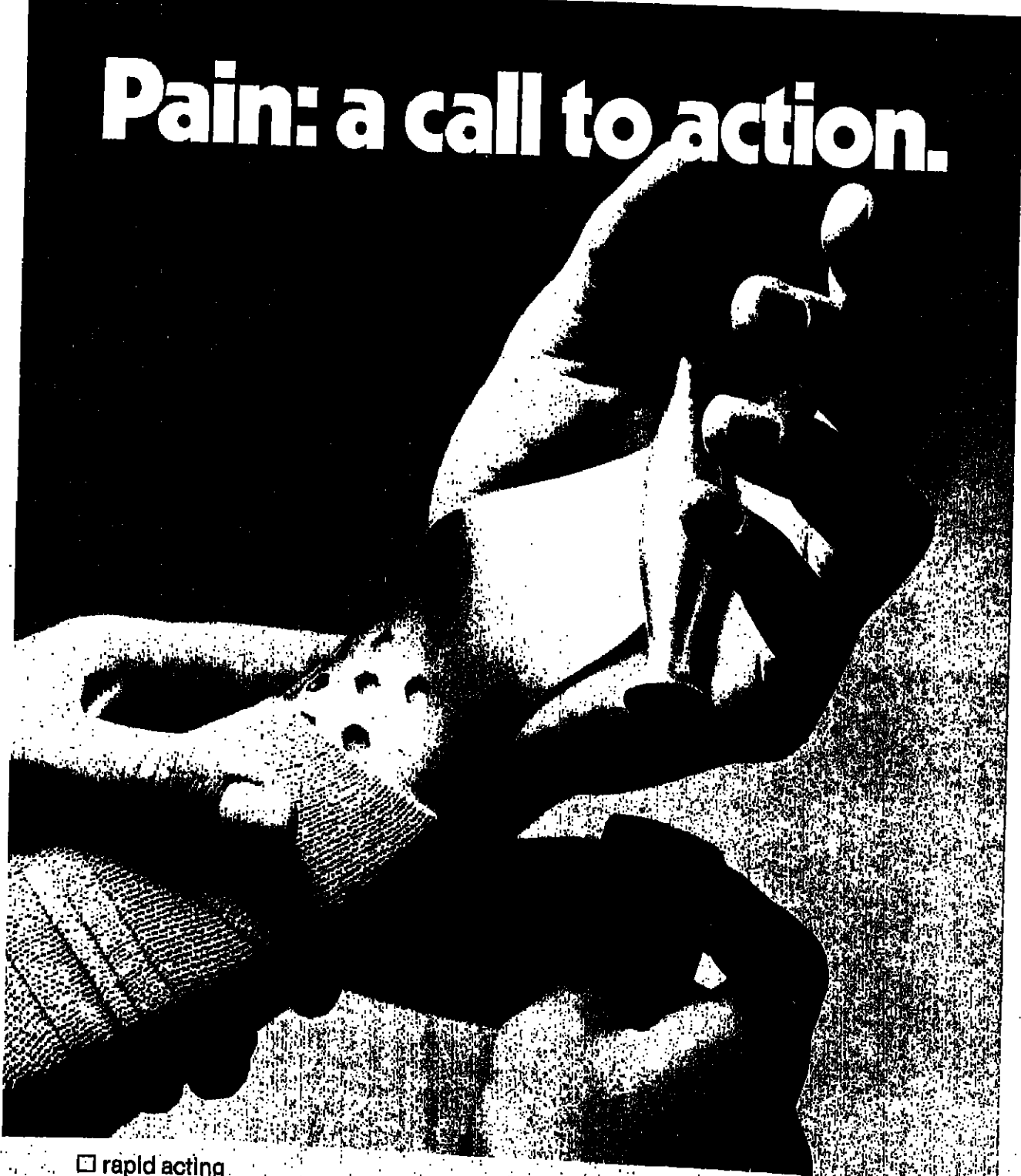
suitable environments found in the Armed Forces and prisons, which afford "conditions of strict isolation and convenient ongoing observation." The need persists for similar studies on other diseases as yet incompletely understood he said, such as viral hepatitis.

Dr. Sabin recalled his own experiences with volunteers over a period of more than thirty years, during which he investigated Japanese encephalitis, Phlebotomus fever, and the polio-virus vaccines. He said that provided the volunteer was fully informed of the possible personal risks and societal benefits of what he was getting into, such experiments were humane, and in fact appealed to the volunteers' best sense of altruism.

Dr. Hubbard agreed on the special value of studies conducted among pris-

Continued on page 7

Pain: a call to action.



Whenever an APC/narcotic is indicated.

Percodan®
Tablets

Each yellow, scored tablet contains 4.50 mg. oxycodone HCl (Warning: May be habit forming), 32 mg. oxycodone hydrochloride (Warning: May be habit forming), 224 mg. aspirin, 160 mg. phenacetin, and 32 mg. other inactive ingredients. For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS: Hypersensitivity to oxycodone, aspirin, phenacetin or caffeine.

WARNINGS: Drug Dependence. Oxycodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Habit formation, physical dependence and tolerance may develop upon repeated administration of Percodan, and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, Percodan is subject to the Federal Controlled Substances Act.

Drug or substance abuse: Oxycodone may impair the mental and physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using Percodan should be cautioned accordingly.

Interaction with other central nervous system depressants: Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other hallucinants, sedative hypnotics or other CNS depressants (including alcohol) concomitantly with Percodan may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in pregnancy: Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, Percodan should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in children: Percodan should not be administered to children.

Salicylates should be used with caution in the presence of peptic ulcer or other gastric disorders.

Precautions: Head injury and increased intracranial pressure: The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce cerebral vasodilation which may obscure the clinical course of patients with head injuries.

Acute abdominal conditions: The administration of Percodan to other narcotic may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Severe renal patients: Percodan should be given with caution to patients with marked renal impairment, and those with severe renal impairment or renal failure. Hypertension, hypotension, Addison's disease, and peptic ulcer should be monitored.

Phenacetin has been reported to damage the kidneys when taken in excessive amounts for a long time.

ADVERSE REACTIONS: The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. Some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation and pruritus.

DOSEAGE AND ADMINISTRATION: Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended before in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. The usual adult dose is one tablet every six hours as needed for pain.

DRUG INTERACTIONS: The CNS depressant effects of Percodan may be additive with that of other CNS depressants. See WARNINGS.

Aspirin may enhance the effect of anticoagulants and inhibit the effect of uric acid excretion.

MANAGEMENT OF OVERDOSEAGE: Signs and Symptoms: Serious reaction with Percodan is characterized by respiratory depression, extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe respiratory depression, apnea, circulatory collapse, cardiac arrest and death may occur. The patient should be kept under close observation and resuscitative measures should be initiated as needed. In fatal cases, resuscitative measures should be continued as long as possible.

Resuscitation: Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist, naloxone, or levorphanol are specific antidotes against respiratory depression which may result from overdose or unusual sensitivity to oxycodone, including oxycodone. Therefore, an appropriate dose of one of these antagonists should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of oxycodone may exceed that of the antagonist, the latter should be repeated as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or circulatory depression.

Supportive measures: Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Safe handling may be needed in removing unabsorbed drug.

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Tablets

Each yellow, scored tablet contains 4.50 mg. oxycodone HCl (Warning: May be habit forming), 32 mg. oxycodone hydrochloride (Warning: May be habit forming), 224 mg. aspirin, 160 mg. phenacetin, and 32 mg. other inactive ingredients.

See facing page for Brief Summary

See dosage and administration section of Brief Summary

- rapid acting
- effective, reliable oral analgesia
- in moderate to moderately severe pain
- oxycodone, the principal ingredient of Percodan, is one of the more readily absorbed oral narcotic analgesics
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Whenever an APC/narcotic is indicated.

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Wednesday, April 16, 1975

Polish Venereologists Said To Show Punishing Attitude

By JAMES MAGEE

Medical Tribune World Service

GENEVA—Polish physicians who specialize in venereal disease take a stern view of their patients, according to a survey of their attitudes.

Prison sentences, compulsory work camps, fines, police surveillance, and other penalties were among proposals put forward to deal with the problem, sociologist Jan Kelus, of Warsaw Medical Academy Institute of Venereology, told a W.H.O. meeting here on health education in the control of sexually transmitted diseases.

Of 144 VD specialists who replied to a questionnaire, nearly 68 said that a person with VD who avoided medical help should be sent to jail. Similar punishment was suggested for prostitution, homosexuality, and infecting another person with VD.

In fact, Mr. Kelus commented, a person who infects another with VD is already liable to imprisonment under Polish law, but this is never enforced. A person who does not seek medical aid is liable only to a fine.

Mr. Kelus said another finding in the survey was that the venereologists unconsciously sought to fit patients into a stereotype. In their replies, they indicated that their patients were mainly: alcoholics, persons "on the fringe of society," persons who were out of work or frequent job-changers, prostitutes or their associates, criminals, and juvenile

delinquents. In addition, one in four of the respondents described his patients as of low education and economic achievement.

In an attempt to check these views against reality, Mr. Kelus and his colleagues selected two groups from the population. One group consisted of 180 persons (86 men and 94 women), of whom 110 had contracted gonorrhea at some time and 70 syphilis. The group was then compared across a range of social parameters with a control group of 665 persons—368 men and 297 women chosen randomly from the voters' lists—who had never had a sexual infection.

No Difference in Education

The investigators found that in terms of education, social ranking, and income, there was no difference between the two groups. The male ex-patients differed from the probability sample in only two ways: they were more often drawn from urban areas, and they less frequently described themselves as regular churchgoers.

Slightly more marked differences were found in the group of women ex-patients. They tended to have relatively lower education, more of them were unskilled workers or low-ranking office staff, and they were more frequently divorced.

The percentage of unemployed was the same in both groups for both sexes.

Adult Blood Found No Aid to RDS Prematures

Medical Tribune World Service

WINNIPEG, MAN.—Contrary to previous reports, exchange transfusions in which infant blood is replaced with fresh adult blood are of no value in reducing the mortality of premature infants with respiratory distress syndrome or those with very low birth weight, a study presented at the annual meeting of the Royal College of Physicians and Surgeons of Canada has indicated.

Conducted by Drs. S. A. Bustamante and K. E. Scott, of Dalhousie University and Grace Maternity Hospital, Halifax, N.S., the study showed that "E.T. made no difference in total plasma, blood pressure, need for mechanical ventilation, or survival" between E.T. recipients and controls.

Because fetal blood has a greater oxygen affinity than adult blood, the latter may speed oxygen delivery to tissues in infants with R.D.S., Dr. Bustamante said.

Exchange transfusion might also be expected to increase plasma protein or blood pressure, he said, adding that low levels of both are associated with infants dying of R.D.S. when compared with survivors.

"The study was designed to include 40 premature infants on the basis of birth weight of less than 1251 Gm. or severe respiratory distress syndrome," Dr. Bustamante explained. "Every infant that met our criteria for the study was assigned to either E.T. or control group by envelope randomization."

The exchange transfusions were carried out within the first eight hours in

the underweight infants, the blood was less than 48 hours old and its plasma was taken off until the hemoglobin was 14 to 16 Gm./100 ml., Dr. Bustamante said.

No Significant Differences

Exchange transfusions made no significant differences between the two groups when compared for respirator survivors, survival rates of low-weight infants, time lapse between entering the study and recovery in survivors, blood pressure, or total plasma, the investigators reported.

Because of envelope randomization, the two groups were also comparable in

weight, gestational age, age in hours when R.D.S. became severe, sex, and mean aortic pressure. Blood pressure and total plasma were higher in survivors, but this is generally true without exchange transfusion, it was noted.

"The results show that the mortality of both groups was identical, with survival rate of 65 per cent, which is about what is expected for a population like the one we selected," Dr. Bustamante said.

"Informed consent was obtained from one of the parents before E.T. was carried out," he noted. "Every parent we approached accepted to enter his or her child in the study."

Perforating Ulcers of Ileum Are Reported In Infants Without Necrotizing Enterocolitis

Medical Tribune Report

NEW ORLEANS—In the past, perforation of the small bowel in early infancy invariably has been associated with necrotizing enterocolitis (NEC). Now Columbia University physicians have reported a 20-year series of 12 newborn babies, mostly premature, who developed perforating ulcers of the ileum in the absence of evidence of NEC. A 13th patient did not have a perforation but showed significant bleeding from the gut.

Dr. H. J. Wigger told the Pediatric Pathology Club here that only five of the ulcer patients at Babies Hospital, New York, died, compared with 47 of 58 infants with NEC seen during the

same period. The postoperative deaths of the ulcer babies resulted from gram-negative infections.

Eleven of the 13 patients had onset of symptoms not later than the sixth day of life, the mean being 2.5 days. Surgery was performed at the mean age of 3.9 days.

All ulcers were found at the antemesenteric border of the ileum, the mean distance from the ileocecal valve being 13.8 cm. The ulcers, numbering one to four, were confined to a small area, and the length of bowel resected averaged only 11 cm., ranging from 1 to 32 cm.

Dr. W. W. Goodhue participated in the study.

Nonaggressive Kayak



Prof. Asen Balikel of Montreal shows a kayak once used by the Netsilik Eskimos, a society believed by anthropologists to be one of the least aggressive societies ever observed, on "Aggression: The Explosive Emotion." This was the second program in "The Thin Edge," a new WNET series on mental health examining depression, aggression, guilt, anxiety, and sexuality.

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CLINICAL NEWS NOTE: "We concur with the literature that the underlying disease is determining in most cases, but at the same time, we concluded that if one can prevent some of the infections...then one can reduce mortality as well as morbidity..." (Dr. Larry D. Edwards, discussing infection control efforts at Chicago's Presbyterian-St. Luke's Hospital, see page 1.)

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Medical Tribune

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EDITORIAL CAPSULES

...brief summaries of editorials or comments in current medical and scientific journals.

Risk Factor Reappraisal

"Within a decade we should learn the results of National Heart and Lung Institute studies of reducing lipids in certain lipid disorders and of controlling hypertension; we should also have data on the promising possibility that control of a combination of three major risk factors may affect the course of coronary disease. If risk factor interventions prove successful, and if these measures were then applied to the entire population it would appear that at best only about 5 to 20 percent of cases could be controlled. If intervention trials were implemented to control risk in the genetically prone high-risk offspring in infancy, possible benefits would not be learned until that population reached the age of clinical manifestations, 50 to 65 years later.

"These considerations suggest an urgent need for new fundamental research and reappraisal of existing experimental and clinical studies, including national population research. Perhaps future studies should investigate in man immunologic and other factors that cause accelerated obstruction of the transplanted veins used in coronary or femoral bypass surgery, and galloping atherosclerosis in the transplanted heart.

"Imaginative investigators might well look for other likely causes of arteriosclerosis.

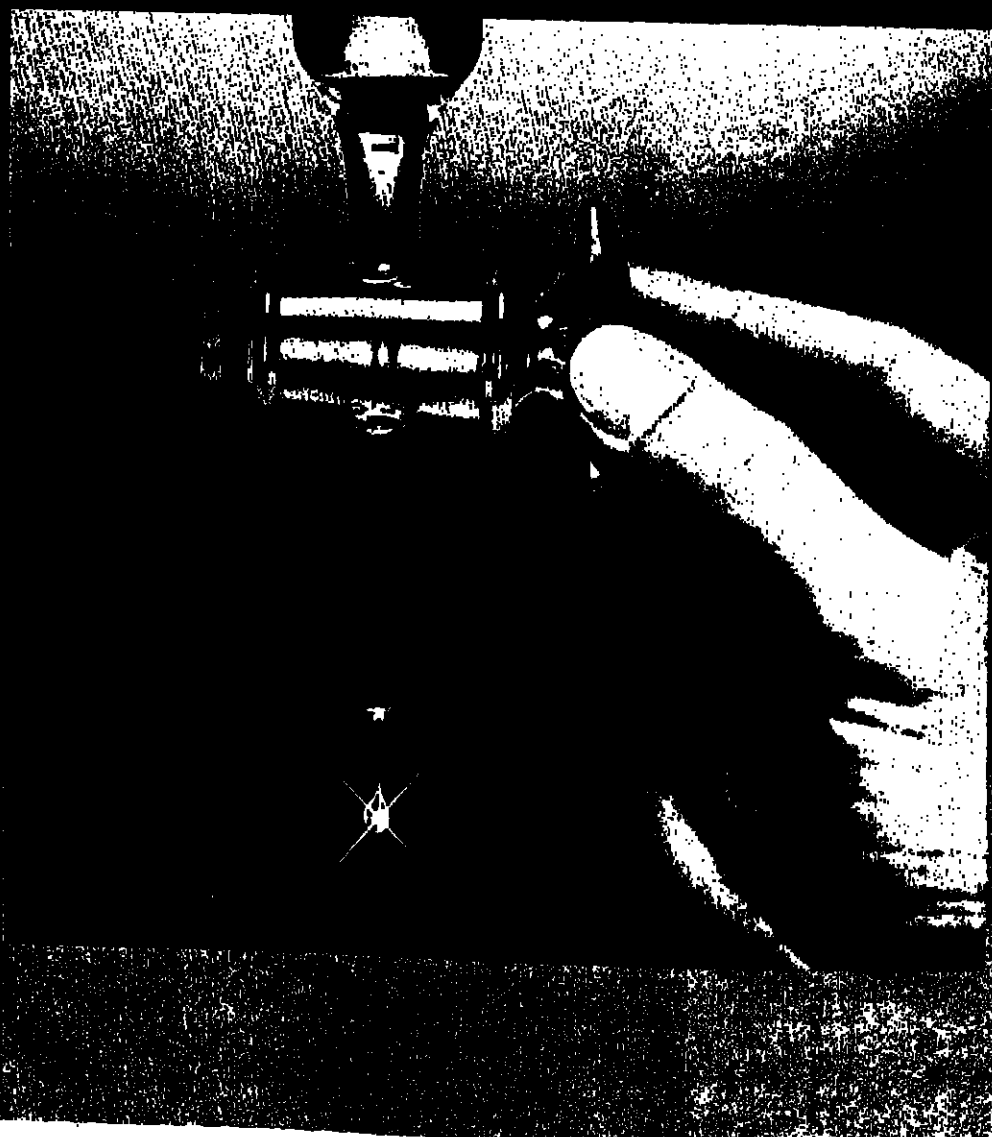
"...It was Einstein's famous equation $E = mc^2$ that provided a major step toward the development of nuclear energy. As yet, we do not appear to possess a formula for the basic genesis of the arteriosclerotic lesion and its prevention because we do not understand the basic underlying mechanisms or how various risk factors influence the progress of the lesion to bring about clinical disease. This lack of knowledge makes it difficult to provide rational programs for prevention and treatment.

"If the multiple risk factor trials fail to prevent the progress of arteriosclerosis, health planners may be reduced to a state of scientific bankruptcy. In planning the defense of a country, the military plan for all future eventualities, including possible failure; the scientific community should also have plans under way in case multiple risk factor trials fail.

"It appears that our nation's overconfidence in present risk factor concepts is impeding development of other promising preventive approaches. Because it will take years to dislocate and relocate the human resources for a new major multidisciplinary attack on the problem of arteriosclerosis, we plead that our Congress provide the highest priority of funding to encourage a more massive research attack now. . . . Where are the alternate plans for defense against our nation's biggest killer?" (Editorial, *Eliot Corday, M.D., F.A.C.C. and Stephen Richard Corday, M.D. Am. J. Cardiol. 35:330, Feb., 1975*)

Esimil...begins with a thiazide

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg



Esimil

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

INDICATIONS

Hypertension. (See box warning.)

WARNING: This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

CONTRAINDICATIONS: Guanethidine: Known or suspected pheochromocytoma; hypersensitivity; frank congestive heart failure not due to hypertension; use of MAO inhibitors.

Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in otherwise healthy pregnant women with or without mild edema is contraindicated and possibly hazardous.

ADVERSE REACTIONS: Antihypertensives are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with all drugs and their combinations before prescribing, and patients should be warned not to deviate from instructions.

Guanethidine

Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning or evening. To help prevent fainting, warn patients to all or lie down with onset of dizziness or weakness, which may be particularly severe during the initial period of dose adjustment and with postural changes. This potential occurrence of these symptoms may require alteration of previous daily prolonged standing or exercise while taking the drug.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression. If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer reduced dosage and have oxygen, atropine, and IV solutions ready for immediate use to treat vascular collapse. Vasoconstrictors and IV solutions ready for immediate use should be used with extreme caution in patients on guanethidine because of the possibility of augmented response and the greater propensity for cardiac arrhythmias.

Dosage requirements may be reduced in presence of fever. Exercise special care when treating patients with a history of bronchial asthma, as their condition may be aggravated.

Hydrochlorothiazide: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid

and electrolyte imbalance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potential occurs with ganglionic or peripheral adrenergic blocking drugs. Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Usage in Pregnancy: Guanethidine: The safety of guanethidine for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Nursing Mothers: Thiazides cross the placental barrier and appear in cord blood and breast milk.

PRECAUTIONS: Guanethidine: The effects of guanethidine are cumulative over long periods. Initial dose should be small and increased gradually in small increments. Use very cautiously in hypertensives with renal disease and nitrogen retention or rising BUN levels; coronary disease with insufficiency or recent myocardial infarction; cerebral vascular disease, especially with encephalopathy. Do not give guanethidine to patients with severe cardiac failure except with extreme caution.

In incipient cardiac decompensation weight gain or edema may be avoided by the administration of a thiazide. Remember that both digitalis and guanethidine slow the heart rate.

...because it is the standard initial therapy—the logical foundation upon which to build. And we picked hydrochlorothiazide, the most widely prescribed diuretic-antihypertensive, which we

...added to perhaps the most effective antihypertensive available, guanethidine...

to create a logical team of therapeutic activities
...for controlling moderate to severe hypertension.

to provide an alternative therapy
...which often controls hypertension in patients not responding to sedatives, diuretics, rauwolfia-thiazides, or other centrally acting inhibitors alone or in combination.

to avoid exacerbating the problem of mental depression
...because Esimil contains no reserpine.

to encourage patient compliance
...because Esimil usually works in once-a-day dosage.

Like all antihypertensives, Esimil should be given with caution in the presence of severe coronary insufficiency or recent myocardial infarction.

Dissatisfied with your present antihypertensive therapy? Why don't you start with the same effective components we did, and when your carefully titrated dosage matches ours—switch to Esimil.

titrate to Esimil

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone.

Amphetamine-like compounds, stimulants (eg, epinephrine, methylphenidate), tricyclic antidepressants (eg, amitriptyline, imipramine, desipramine) and other psychopharmacologic agents (eg, phenothiazines and related compounds), and oral contraceptives may reduce the hypotensive effect of guanethidine. Discontinue MAO inhibitors for at least one week before starting guanethidine.

Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hypotension, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.

Hypokalemia: may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe hypokalemia is present, or during concomitant administration of steroids or ACTH.

Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver diseases or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening.

In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest following thiazide administration. Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathetic patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS: Guanethidine: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions due to unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (may be severe). Other common reactions—(inhibition of ejaculation, fluid retention, edema, congestive heart failure, other less common reactions—dyspepsia, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, ptosis of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (anginal), chest parasthesias, nasal congestion, weight loss, asthma in susceptible individuals. A causal relationship has not been established for a few instances of anemia, thrombocytopenia and leukopenia have been reported.

Hydrochlorothiazide: Gastrointestinal—nausea, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. Central Nervous System—drowsiness, vertigo, paresthesias, headache, xanthopsia. Dermatologic—Hypersensitivity—purpura, photosensitivity, rash, urticaria, necrotizing angitis, Stevens-Johnson syndrome, and other hypersensitivity reactions. Hematologic—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Other—Hypersensitivity reactions, hyperuricemia, muscle spasm, weakness, restlessness, mya, muscle pain, glycosuria, hyperuricemia, severe adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSEAGE: As determined by individual titration (see box warning).

Noting 10 mg guanethidine monosulfate present in Esimil is equivalent to 8.4 mg guanethidine sulfate USP.

Before starting therapy, consult complete product literature.

HOW SUPPLIED: Tablets (white, scored), each containing 10 mg guanethidine monosulfate and 25 mg hydrochlorothiazide; bottles of 100.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

C I B A

'Right to Volunteer' For Research Gets Panelists' Support

Continued from page 2

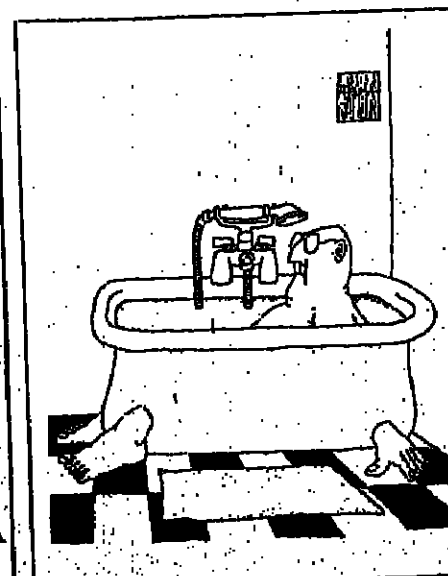
oners and soldiers, but stressed the importance of guidelines to reduce to a minimum any element of coercion. In the Michigan prison system where he has been involved in the testing of drugs for fifteen years, Dr. Hubbard said there is an elaborate procedure of full explanation to all volunteers of dangers, discomforts and civil rights. Moreover, volunteers are not solicited, and they are expressly told that their participation will have no bearing on parole eligibility. All drug research programs must be unanimously approved by a Protection Committee comprising two biomedical scientists, three physicians, and two lawyers, one of whom must be associated with prisoner advocacy. The prisoner has the right to withdraw from the study at any time.

According to Dr. Hubbard, since 1964, 12,000 Michigan inmates have participated in drug research studies, with one death from "stroke" of a subject serving as a placebo control, and nine illnesses without sequelae.

Full Disclosure Stressed

Dr. Katz, focusing on problems of experiments on the poor, also emphasized the importance of "full, total disclosure" if such experiments are to be humane and truly progressive. While not questioning the need for controlled clinical trials, he cited various abuses by investigators, who had lost sight of their subjects as fellow human beings, which had also been brought to the panel's attention by Mr. Bronstein. However, Dr. Katz warned against the wholesale exclusion of any group from voluntary participation—such exclusion, he said, stemmed from the same "stereotypical" prejudices that had led to "degrading" abuses.

"It is equally demeaning to assert that persons' consent should be rejected because, if they were wiser or more rational, they would have made different decisions, as it is to assert that their consent should not be trusted because, if they only were richer, they would have chosen differently," Dr. Katz said. "Ultimately we must bow to the best decisions persons can make as they are situated."



Medical Tribune Reports

Eight workers developed paroxysmal cough; and deep cyanosis, tachycardia, diaphoresis, and dizziness were observed in five others, Dr. Andrascch told the 31st annual meeting of the American Academy of Allergy here. In addition, other workers in the study reported shakiness, severe burning in the nose and throat, headache, nausea, muscle ache, rhinorrhea, weakness, vomiting and hoarseness, he said.

"Dryness and burning of the mucous membranes, severe headache, extreme irritability and nausea were frequent



Although the fumes from the heated meat labels have still not been chemically identified, the adhesive backings are known to contain miscellaneous elastomers, thermoplastic copolymers, styrene butadiene copolymers, styrene acrylonitrile copolymers, polyphenylene oxides, polysulfones and phthalic acid plasticizers, the Oregon researcher said. Fumes produced when PVC wrappings are sliced by hot wire cutters, include carbon monoxide, carbon diox-

The Oregon study, supported by the local Meat Cutter's Union, followed a survey of 67 meatwrappers in the Portland area. Of those who responded, 57 per cent reported "moderate to severe respiratory symptoms," while a smaller number complained of head-

New film cutting machines seem to be reducing the PVC hazard at this time, Dr. Andrasch concluded, suggesting that the hazards from meat label fumes could also be minimized through the expanded use of recently developed automatic labelling machines.

A black and white photograph of a still life arrangement. In the foreground, a large, dark, rounded object, possibly a hat or a piece of fabric, is draped over a surface. Behind it, a bouquet of flowers, including roses, is visible. The background is a textured wall with a dark, diagonal line running across it.

Zim company, the Israeli shipping line, has installed ship-to-shore electrocardiography on one of its vessels in what is believed to be the first trial of its kind. The machine is connected by radiotelephone to a monitor at Rambam Hospital in Haifa. The initial test, carried out when the ship was 600 miles off Haifa, was reported to have produced surprisingly clear results.

Winthrop Laboratories, New York, N.Y. 10016 **Winthrop**

See important product information for adverse reactions, patient selection, prescribing and precautionary recommendations.

Bill number 86, introduced by Senator George Moscone, D.-San Francisco, was recently passed by a vote of 22-1 in the State Senate. John Jervis, aide to Sen. Moscone, told MEDICAL TRIBUNE that he expects smooth sail-

Several California physicians who find fault with the Moscone proposal concede that it is virtually assured passage. Their main objection concerns the composition of the Advisory Board.

Her view is shared by Dr. George Wong, Jr., a family practitioner in Long Beach, who, like Dr. Lee, has extensive training in acupuncture and uses it as an "adjunct mode" in his practice. Dr. Wong is Chairman of the Acupuncture Research Institute of the American Association, a non-profit organization of physicians interested in

Continued on page 23



What a difference a day can make

Your counsel and reassurance—and Ritalin.

A logical first step in treating mild depression* and often all that's needed to bring quick symptomatic relief.

Indeed, your patient may be-

gin to feel better within hours—her spirits boosted, her mood brightened. A single prescription may be all that's needed.

Ritalin is usually well tolerated even by older or convalescent patients. Note, however,

that it is not indicated in the more severe depressions.

But whenever depression is mild, think of Ritalin—so your patient has a better chance of waking up to a brighter tomorrow.

Ritalin

(methylphenidate)

acts quickly to relieve symptoms
in mild depression

*This drug has been evaluated as possibly effective for this indication. See brief prescribing information.

Ritalin® hydrochloride (methylphenidate hydrochloride) TABLETS

INDICATION

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indication as follows:
"Possibly" effective: Mild depression
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Marked anxiety, tension, and agitation, since Ritalin may aggravate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS

Ritalin should not be used in children under six years, since safety and efficacy in this age group have not been established.

Sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available. Although a causal relationship has not been established, suppression of growth (ie, weight gain and/or height) has been reported with long-term use of stimulants in children. Therefore, children requiring long-term therapy should be carefully monitored.

Ritalin should not be used for severe depression of either exogenous or endogenous origin or for the prevention of normal fatigue states.

Ritalin may lower the convulsive threshold in patients with or without prior seizures; with or without prior EEG abnormalities, even in absence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. If seizures occur, Ritalin should be discontinued. Use cautiously in patients with hypertension. Blood pressure should be monitored at appropriate intervals in all patients taking Ritalin, especially those with hypertension.

Drug Interactions
Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and (tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustment of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy
Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence

Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS

Patients with an element of agitation may react adversely; discontinue therapy if necessary. Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity (including skin rash, urticaria, fever, arthritis, exfoliative dermatitis, erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura); anorexia; nausea; dizziness; palpitations; headache; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking this drug: leukopenia and/or anemia; a few instances of scalp hair loss.

In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

DOSEAGE AND ADMINISTRATION

Adults
Administer orally in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Dosage will depend upon indication and individual response.

Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. The few patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

HOW SUPPLIED

Tablets, 20 mg (pale green, scored); bottles of 100 and 1000.
Tablets, 10 mg (pale green, scored); bottles of 100, 500, 1000 and Accu-Pak blister units of 100.
Tablets, 5 mg (pale yellow); bottles of 100, 500 and 1000.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

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C I B A

Wednesday, April 16, 1975

MEDICAL TRIBUNE

11

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Genetic Engineering

THE INTERNATIONAL CONFERENCE ON Recombinant DNA Molecules, which met in late February in Asilomar, Calif., has drawn up a list of recommendations on precautions to be taken by investigators working in the field of genetic engineering (see page 5). Technical skills now available make it possible with the use of certain enzymes to cleave DNA at specific sites and join DNA from animal viruses with bacterial DNA or with viral DNA. The possibilities include illumination of the very basics of gene action.

But a year and a half ago, the potential hazards of "new kinds of hybrid plasmids or viruses, with biological activity of unpredictable nature" was raised at the 1973 Gordon Conference on Nucleic Acids. A Committee on Recombinant DNA Molecules, chaired by Professor Paul Berg of the biochemistry department at Stanford University, was formed in 1974 and in July called for a voluntary suspension of certain types

of genetic manipulation until a conference of workers in the field could be held to spell out precautions and tabus.

The precautions discussed at the conference include the high skills of the investigators themselves, the careful laboratory practices needed, and the use of biological barriers, such as organisms capable of survival only in the special environments of laboratories and not in natural environments.

Nobel Laureate Joshua Lederberg has expressed the fear that safeguards and precautions "that are entirely appropriate for certain risks might be prematurely rigidified into a set of bureaucratic regulations that might be very readily enforced beyond the domain of their reasonable application." That is a more than reasonable fear but, at this time, the precautions and the safeguards are in the hands of the investigators themselves. It is up to them to keep control in their own hands and out of the hands of bureaucrats.

Solving the Riddle of Diabetes Mellitus

IT IS NOW 54 years since Banting and Best demonstrated that an extract of the islet tissue of the pancreas can lower the blood sugar of the diabetic dog. Although the successful preparation of insulin extracts seemed at first to have solved the riddle of diabetes mellitus, this enthusiastic belief soon waned. Indeed, in the past quarter of a century, the puzzling questions about the etiology and pathogenesis of diabetes have multiplied rather than diminished as the techniques for investigating the disease have become more sophisticated and precise.

There are many reasons why the definition of diabetes mellitus as simply a disorder resulting from a relative or absolute deficiency of insulin secreted by the beta cells of the pancreas is unsatisfactory. For the past several years, Dr. Roger H. Unger of the Veterans Administration Hospital in Dallas, Texas, and the U. of Texas Southwestern Medical School, has championed the notion that the disease is a bihormonal disease, "which holds that the major consequence of absolute or relative insulin lack is glucose underutilization and that absolute or relative glucagon excess is the principle factor in the overproduction of glucose in diabetes."

There is powerful evidence in support of this concept. The alpha cells of the pancreas secrete glucagon, which is

known to be a hyperglycemic hormone. There has been ample demonstration since the late 1960's that every form of diabetic and non-diabetic hyperglycemia investigated "is accompanied by relative or absolute hyperglucagonemia."

Since the discovery of somatostatin, the hypothalamic growth hormone-release-inhibiting factor, it has been found to suppress both glucagon and insulin secretion. A series of brilliant investigations in Dr. Unger's laboratory and in a number of independent laboratories have demonstrated that hyperglycemia in dogs made insulin-deficient by alloxan or total pancreatectomy is abolished by somatostatin injection.

Dr. John E. Gerich and his colleagues at Dr. Peter Forsham's laboratory at the U. of California in San Francisco have recently reported that somatostatin injection in insulin-dependent diabetics reduced their plasma glucagon—and hyperglycemia as well. As the investigators state: "The present findings have important therapeutic implications." What is needed is a preparation of somatostatin with a prolonged half-life. The exciting and intriguing possibility is that failure to prevent microangiopathy and atherosclerosis in diabetics by insulin therapy may be turned to success with the addition of somatostatin to the therapeutic regimen. Time will tell.

Hepatitis B Virus Carriers

CLINICAL QUOTE: "The significance of hepatitis B infection in early life lies...also in its importance in the genesis of prolonged carriage of hepatitis B virus. Zuckerman and Taylor (1969) described a well-documented healthy former blood donor carrying

hepatitis B antigen for at least 20 years. That a reservoir of chronic carriers may become established among children is, therefore, a cause for the utmost concern." (Dr. Arie Zuckerman, at a March of Dimes-National Foundation symposium on infections.



"I'll tell you something else I'm learning to live with! Doctors who say, 'Learn to live with it!'"

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LETTERS TO TRIBUNE

Carotid Artery Palpation

I must take exception to one statement of Dr. Edwin Beven's (MT, Mar. 5).

Noninvasive or not—any palpation, compression, movement of adjacent structures, etc.—concerning a carotid artery with even minor stenosis cannot be considered a "No-Risk Method."

While the risk may be slight, the possibility of causing sudden, complete occlusion or cerebral embolization does exist and should be taken into consideration before even getting close to a patient's carotid artery. The presence of anomalous circulation, stenosis of other vessels elevated lipoproteins, prior T.I.A.s and a variety of other factors will, of course, increase the risk.

DONALD M. POSNER, M.D.
Canaan, Vt.

HARRY WELKER
New York

New Laws Needed?

Dr. David Nathan is quoted (MT, Feb. 12) as follows "It never occurred to us that society would be worried that we will not maintain life." This must certainly strike a new low in what used to be called a "life science" of medicine. Poor Dr. Nathan is so preoccupied with what he sees on the other end of his microscope that he forgets that he is in the business of saving lives.

Irresponsible ivory tower pseudoscientists who have used unborn children as lab animals in vivisection-type experiments have created the need for new laws. They would like to use "hostility to abortion" as their whipping boy but the real culprit is their own ignorance of the Declaration of Helsinki.

THOMAS J. EGAN, M.D.
Chicago

Telling the Patient

Right on for Dr. Eli Friedman "Panelists Disagree on How Much To Tell Patient," (MT, Mar. 12)!

For the moment let us lay aside the complex and tricky question of whether or not to inform a patient if he or she is dying. Rather, let us consider the non-comatose patient of average intelligence. Even in the best run hospitals mistakes are made, orders scribbled illegibly on a patient's chart, residents and nurses carelessly or too hastily briefed on medications and/or general management of a case.

If the physician will take the time to explain carefully to the patient what he is being treated for, what the medication is, and how and when it should be

administered, that patient will damned well be his own watchdog to see that his doctor's orders are carried out to the letter.

I personally have, in two highly respected medical institutions, refused attempted treatments which I knew were not ordered by my physician. Since I have the benefit of having been a medical journalist for 15 years I knew one procedure would have resulted in a fast trip to the intensive care unit, if not the morgue.

As doctors you owe that to your patients. Tell them to yell their heads off if anyone attempts treatment counter to your instructions. Who knows? If that were made standard procedure there might be a marked drop in malpractice suits.

Endorsing Euthanasia?

The American Association of Pro Life Obstetricians and Gynecologists, comprised of members of our specialty from throughout the entire United States, wishes to make some observations regarding the Edelin verdict.

The Supreme Court decision of January, 1973 removed abortion from the criminal code and set it outside the law by making the mother and her physician entirely responsible for the destruction of human life. No mention was made in the Supreme Court decision as to what happens to the infant born alive and struggling for survival. As there have been hundreds, and possibly thousands, of these sadly unfortunate infant victims, sound medical practice and compassion should motivate all of us to render these babies the best possible medical care for survival. As obstetricians and gynecologists, we have all seen infants of less than two pounds birth weight survive and do well when given the proper care. Why shouldn't we feel obligated to render the same care to the survivor of a miscalculated abortion procedure that we render to the infant in a normal delivery?

If the obstetrician has the right to destroy the live-born infant in an abortion procedure, would he not have the same right to extinguish the life of a new-born infant with a congenital defect whose mother may not want him?

The acceptance of this principle surely would, in fact, be providing a legal endorsement of euthanasia.

MATTHEW J. BULFIN, M.D.
President
Lauderdale-By-The-Sea, Fla.

Nitroglycerin Reported 'Consistently Beneficial' in Infarction

Continued from page 1

sign of hypotension and reflex tachycardia they have also administered the vasoconstrictor phenylephrine to mitigate these two side effects.

In general, Dr. Epstein noted, M.I. patients fall into two subgroups. One consists of those in heart failure, with elevated pressures and inadequate pumping action. "In this group, nitroglycerin appears to be very effective in reversing the manifestations of heart failure," Dr. Epstein said. "The high pressures that build up in the lungs decrease to normal very abruptly after nitroglycerin administration and the heart starts pumping more effectively. That's not new; these effects have been demonstrated by groups at Cedars of

Lebanon Hospital in Los Angeles, at Massachusetts General Hospital, and at Johns Hopkins. But what we have found in addition is that the size of the infarct, the amount of muscle damaged, is significantly reduced by treatment with nitroglycerin."

Non-Heart-Failure Group

The second subgroup of patients are those who have suffered a heart attack, Dr. Epstein continued, who have damaged muscle, but are not in heart failure. These patients are not usually treated, he said, "but nevertheless about 10 per cent of them die in hospital and another 10 per cent die within a year, so it is not a benign disease. In this subgroup of patients who have never been

treated before, we found exactly the same thing. We didn't get them out of failure, because they weren't in failure to begin with, but we found that the combination of nitroglycerin and phenylephrine reduced infarct size."

Dr. Epstein noted also that it is the second subgroup of patients that most often requires the phenylephrine to reverse the side effects of the nitroglycerin. And in the future, he said, he and his associates plan to give the nitroglycerin intravenously so it can be monitored more readily and more precisely.

On the basis of their experience with animals, Dr. Epstein said he thinks the nitroglycerin exerts its beneficial effects in two ways: by increasing the amount of blood delivered to the ischemic area

via the collateral system, and by reducing the size of the heart chamber, thus decreasing myocardial tension and oxygen requirements.

Dr. Epstein is working with Dr. Kenneth M. Kent, Dr. Robert E. Goldstein, and Dr. David R. Redwood, of the N.H.L.I. Cardiology Branch, and Drs. Barrie Levit and Norman Cagin, of Flower and Fifth Avenue Hospitals, New York. Dr. Jeffrey S. Borer, who is in London on sabbatical leave from the N.H.L.I., is also participating in the trials.

Whether the treatment increases long-term survival is yet to be ascertained, Dr. Epstein said. But he thinks it has "enormous potential" and that long-term studies should be mounted. Dr. Epstein's animal studies are described in the January 2, 1975, *New England Journal of Medicine*, and preliminary clinical data appear in the April *Journal of Clinical Investigation*. Dr. Borer will present the full clinical report to the American Society of Clinical Investigation in May.

Hepatitis B Virus Pool in Newborn Seen Building Up

Continued from page 1

and sponsored by the National Foundation-March of Dimes.

An evaluation of recent studies makes it clear, he emphasized, that both transplacental and perinatal transmission of hepatitis B infection from mother to child may take place in spite of older notions to the contrary.

Dr. Zuckerman recommends that all antigen-positive mothers be instructed to pay scrupulous attention to personal hygiene when handling their infants. Since there is the possibility of transmission of the antigen via breast milk, he believes breast feeding in these cases should be discouraged.

Control Attempted in Newborn

Control of hepatitis B infection in the newborn is now being attempted by passive immunization with specific hepatitis B immunoglobulin and by immunotherapy with transfer factor, he commented, adding that safe and effective hepatitis vaccines—"now under development"—are a pressing need.

The limited data available indicate that the frequency of transmission of hepatitis B from mother to infant is highest (76 per cent in one study) when acute infection occurs during the third trimester of pregnancy or early in the postpartum period, and relatively low (10 per cent) if it develops during the first six months, Dr. Zuckerman said. Investigations of transmission by asymptomatic carrier mothers have yielded variable figures but in one Japanese study cited by Dr. Zuckerman eight of 11 infants born to such mothers showed antigen in their sera within six months of delivery and the antigen persisted during prolonged follow-up.

Many of the infants in whom antigen is detected remain clinically well, the virologist said, although some show "prolonged elevation of an enzyme frequently associated with liver damage,"

Control Program Credited With 10% Decrease in Hospital Infections

Continued from page 1

The study, which was conducted at Chicago's Presbyterian-St. Luke's Hospital between 1969 and 1973 and computer analyzed 11,656 occurrences of nosocomial infection, revealed a 10 per cent decrease in hospital infections at a time when more patients susceptible to infection were being admitted, said Dr. Edwards, who was the epidemiologist at the 840-bed hospital during the study period.

"Previous thorough studies have been very short-term and thus hard to interpret because there may be fluctuation in hospital infection rates from month to month," he said.

Nearly \$650,000 a Year Saving

Attributing the decrease to the hospital's active infection control program begun in 1968, Dr. Edwards stated that the program generated a significant reduction in economic morbidity amounting to nearly \$650,000 per year, in addition to saving lives.

"We calculated this figure in the following way," he said. "The average patient stay in the hospital was 11-12 days during the study, varying from year to year. The average stay for patients with hospital onset infections, on the other hand, was 33 days, or an additional 21 days, at an average per diem charge of \$150. Considering that we encountered an average of 2009 patients a year with hospital onset infections and multiplying these figures out, we estimate that the cost to patients and third-party payers for such infections was around \$6,328,350 a year. A 10 per cent reduction in infection rate, therefore, means an average savings of \$630,830 per year. Since the total cost of running our infection control program—including paying the salaries of three full-time nurse-epidemiologists and one half-time physician, as well as the costs of computerization—was around \$75,000 a year, the economic advantage of the program was considerable."

Reduction in Mortality

The study also revealed significant findings with respect to mortality. "One can place patients dying of infection into three categories. In the first, the infection is the primary cause of death; in the second, the underlying disease is primary; and in the third, the infection contributes to but is not entirely responsible for the death. In our study we found that infection was the primary cause in 12.9 per cent of cases, that infection was an associated and contributing cause in 25.9 per cent, and that the underlying disease was primary in 61.2 per cent."

"Thus we concur with the literature that the underlying disease is determining in most cases, but at the same we concluded that if one can prevent some of the infections in the 12.9 per cent category, then one can reduce mortality as well as morbidity."

Looking at hospital onset infections in the context of total hospital mortality, Dr. Edwards indicated that about a fourth of patients who died at Presbyterian-St. Luke's between 1969 and 1973 had an infection of hospital origin at the time of death.

The epidemiological methods that eventually brought about the 10 per cent reduction in hospital onset infections at St. Luke's were scrutinized both during the formal study period and during a brief pre-computer programming study in 1969. "In the earlier study we wanted to validate the effectiveness of the nurse-epidemiologists since many physicians at the time doubted their ability to accurately collect data. In comparing three fellows in the infectious disease section with two nurse-epidemiologists over a two week period we found that the latter were 94 per cent as effective as the former in collecting and classifying data on infections, which is not a statistically significant difference. We specifically restudied this question several times throughout the next four years and found that the nurses were consistently as accurate as the physicians trained in infectious diseases."

"In the earlier study," Dr. Edwards added, "we also wanted to find out how many nurses are needed per number of beds to do the job and how often they need to visit the wards. Basically we concluded that one nurse was required for 300 beds and that they needed to visit the wards twice a week. After it was decided that we needed three nurses for our 840 beds, we hired an additional nurse."

Combined Approach Used

Once a full-blown infection control program was launched at Presbyterian-St. Luke's in 1969, a combined epidemiological and teaching approach was followed. "There are four different approaches that hospitals may take," commented Dr. Edwards. "First, many hospitals merely have a perfunctory infection control committee that meets in order to fulfill accreditation requirements but doesn't really do anything about the endemic level of hospital infections and only becomes active if there is an outbreak. Unfortunately I suspect that this is the most common approach. Second, there is the command approach, in favor of which physicians will argue that we already know what most of the problems are so let's go out and work on those and also be ready to investigate any epidemics that may come up. Unquestionably that approach will lower the infection rate at some sites at some hospitals, depending on the interests of the people who are commanding the commandos, as it were. But it doesn't tell much about whether one is getting a total impact and a uniformly educated hospital staff to reduce the overall problem over the long haul."

"The third approach is what one might call the surveillance approach and implies simply collecting data. This has been much maligned because people should not just collect data and do nothing about it. The fourth approach, and the one we opted for, is the epidemiological one in which you do essentially all of the things that the other approaches do plus actively inform and instruct."

"Something I've always felt strongly about with respect to hospital infections," Dr. Edwards continued, "is that since we have such a large turnover

Role of Community Onset Infections and Hospital Onset Infections in Deaths By Service From 1969 Through 1973

Service	Infection Primary Cause		Infection Associated		Underlying Disease Primary Cause	
	GOI*	HOI**	GOI	HOI	GOI	HOI
Medicine	14.3	9.4	25.2	22.9	60.5	50.7
Surgery	10.6	18.7	18.7	22.0	89.4	82.3
Pediatrics	24.7	24.6	30.8	18.9	24.7	66.8
Newborns	0.0	18.7	33.8	38.3	66.7	66.0
Total Hospital	15.2	12.9	24.8	26.9	60.2	61.2

*GOI = Community Onset Infection; HOI = Hospital Onset Infection.
**GOI = Community Onset Infection; HOI = Hospital Onset Infection.

Mortality Associated With Community Onset Infections and Hospital Onset Infections By Services From 1969 Through 1973

Service	Per Cent of Admissions		Per Cent of Deaths		Number of Infections Per Death	
	GOI*	HOI**	GOI	HOI	GOI	HOI
Medicine	1.7	1.7	22.3	22.8	1.4	1.7
Surgery	0.8	1.1	13.1	42.0	1.2	2.2
Pediatrics	0.4	0.4	22.1	25.0	1.6	2.1
Newborns	0.0	0.1	11.3	5.3	1.4	1.6
Total Hospital	0.8	0.8	18.4	26.2	1.4	2.0

*GOI = Community Onset Infection; HOI = Hospital Onset Infection.
**GOI = Community Onset Infection; HOI = Hospital Onset Infection.

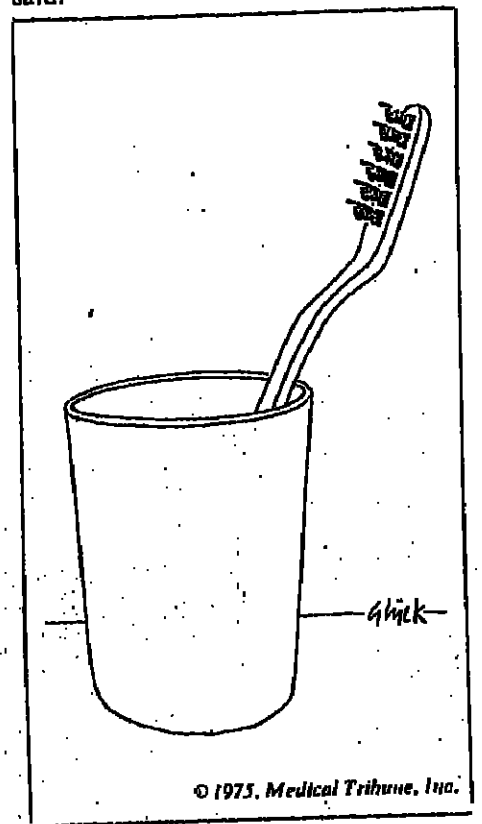
rate of hospital employees today, the key to control isn't so much new knowledge as it is having some ongoing way of continually bringing the problem to people's attention, both in terms of education about how to perform certain procedures and in terms of epidemiological data so one can know whether one is making an impact. If we're not, then push harder in the particular area where we're not making an impact. I don't think one can make reasonable applications unless one knows what is going on in one's own hospital."

80% of Infections at 4 Sites

In the Presbyterian-St. Luke's study it was determined that about 80 per cent of the infections were occurring at four major sites—the urinary tract, lower respiratory tract, surgical wounds and bloodstream. "All of the sites had pretty much the same decrease in infections except for the bacteremias, which actually went up. In 1969 there were 969 urinary tract occurrences compared to 741 in 1973, 665 lower respiratory tract occurrences compared to 651, 520 surgical wound infections compared to 402, and 173 bacteremias compared to 233. The rise in bacteremias, I think, may be due to the fact that the hospital started doing more bowel cancer surgery."

An unusual aspect of the study, and one which requires further investigation, is that it was the first long-term study to look at the interchange between community onset and hospital onset infections. "We defined a community onset infection as one present on admission or coming up in the first 72 hours and not related to a hospital procedure. I don't think we have any hard and fast data on this interchange, but we got some inkling into where we need to look

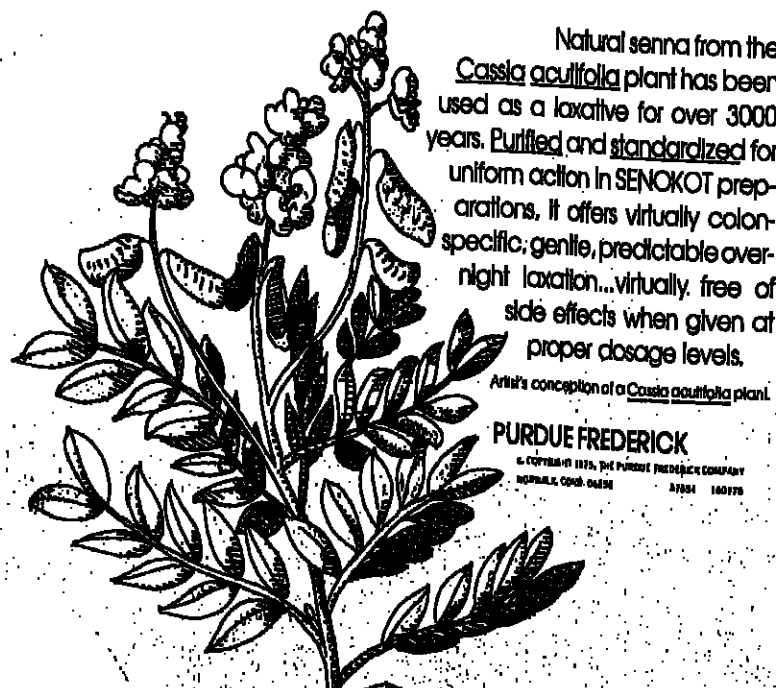
further. For example, it's been well known that hospital personnel tend to have higher carriage rates of organisms like *Pneumococcus* compared to people in the community. Well, we counted several such classical infections that appeared to have their onset in the hospital; so the question is whether there is some interplay going on here that allows for spread of these organisms in the hospital at a greater frequency. We don't know much at all about how viral infections are introduced into and then spread throughout the hospital, and I think we can expect to see a greater research effort in this area," Dr. Edwards said.



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In this age of synthetics
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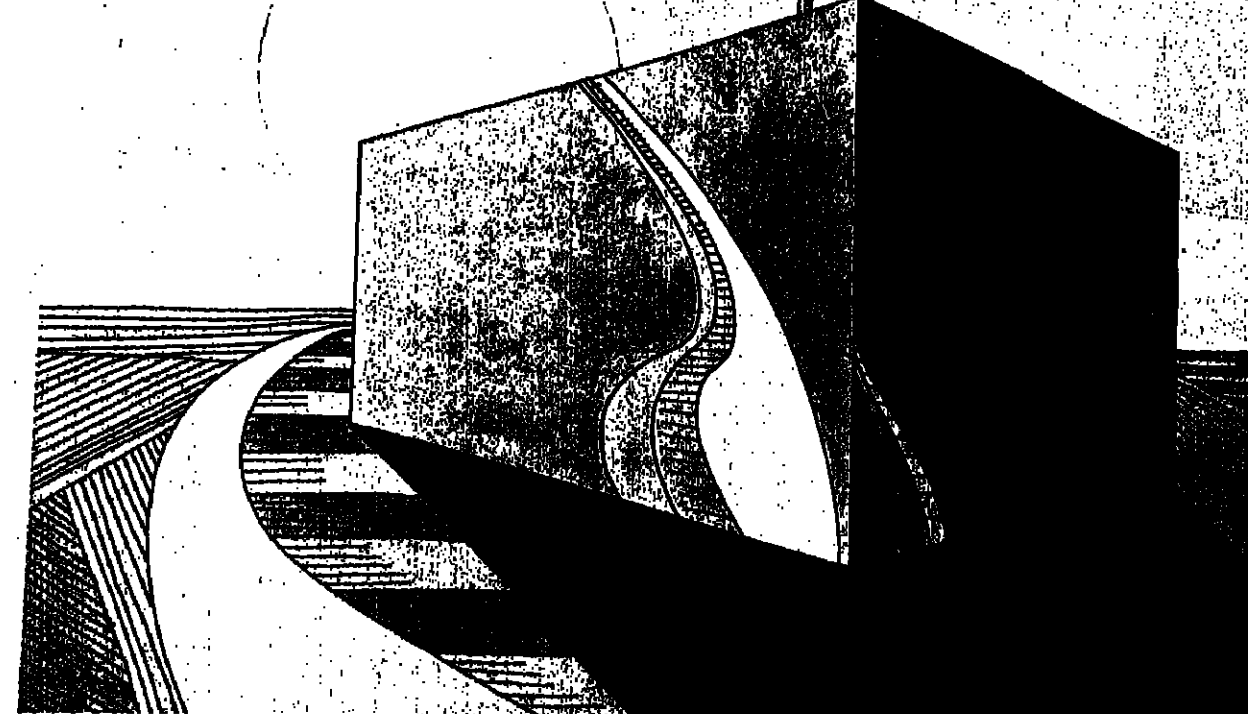
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Artist's conception of a *Cassia acutifolia* plant.

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Many of the infants in whom antigen is detected remain clinically well, the virologist said, although some show "prolonged elevation of an enzyme frequently associated with liver damage,"

Interdisciplinary PG Training Program Set

By MICHAEL HERRING
Medical Tribune Staff

ROCHESTER, N.Y.—An interdisciplinary postgraduate training program at Strong Memorial Hospital utilizing internists, pediatricians, and specialists in the same physical setting—and in some cases operating as a fee-for-service private group practice—will go into full effect as soon as all services are moved into the new ambulatory care wing here, Dr. Warren Glaser, program coordinator, told MEDICAL TRIBUNE.

The program will provide for training at all levels, he said, and make physician services more readily available to all patients in the community, regardless of their ability to pay.

Effective Coordination Sought

"We can't sacrifice the expertise we've gained from so much specialization, but at the same time, there has to be a way to coordinate individual efforts more effectively," he explained. "The beauty of the arrangement at Rochester is that you have both the generalist and the specialists working compatibly and in close proximity."

Dr. Glaser, who is Professor of Medicine and coordinator of ambulatory care, Department of Medicine at the University of Rochester School of Medicine and Dentistry, said that the decision to form the hospital team of group-practice internists and pediatricians, with the backup of subspecialists in each major area, was based on the recognition that "the hospital stands at the center of the ambulatory health care system."

"Ideally," he said, "each person in the community should have access to a personal physician who renders comprehensive care with continuity and who can delegate that care when necessary to the appropriate specialist."

Primary care, he continued, should be medical attention that is "available and accessible" to the patient when he or she needs it. "Primary care should not refer only to the initial visit to a doctor during office hours, but includes empathy, continuity, and treatment that is appropriate to the patient's changing needs," he said.

Integrationist for Subspecialties

"At the same time, it should function to take the load off the emergency-room physician. Finally, the primary care physician is the integrationist for all medical subspecialties that the patient may require."

Dr. Glaser emphasized that the primary care physician at Strong Memorial will function increasingly as a member of a team—"not just with other doctors, but with nurses, social workers, and other medical and paramedical personnel."

"We think that the group practice of general internists and general pediatricians has more appeal," he commented, "because it is a higher level of care, and permits more appropriate referrals within the system."

Dr. Glaser briefly described the new arrangement at Strong Memorial as follows:

"In medicine, we have two or three interns, two assistant residents, and

two associate residents teamed with an attending physician and a licensed practical nurse. The whole team cares for a panel of patients."

In addition, he explained, the interdisciplinary group, together with the house staff, care for the medical clinic and combined clinic patients from the previous arrangement.

"These patients are now considered as one group of hospital patients, and are seen on a private-practice basis. Once a patient is entered into the system, the fees for hospital services and the fee-for-service practice are the same. Patients, no matter how they pay, can be transferred from one group to another. The only difference is in who does the billing."

The internal medicine group is a fee-for-service, private practice group, Dr. Glaser added. "These physicians cover for one another on a team basis."

"The doctor's offices will be in the hospital itself. If hospital patients require care after clinic hours, we use the emergency room. But we don't descend on the emergency room just because we can't provide care elsewhere."

ER Resident on Call

"Rather, the resident in the emergency room acts as the on-call physician in a manner similar to those in the internal medicine group covering for one another. Obviously, we can't know all the patients, but we can provide care, based on the fact that this is a recog-

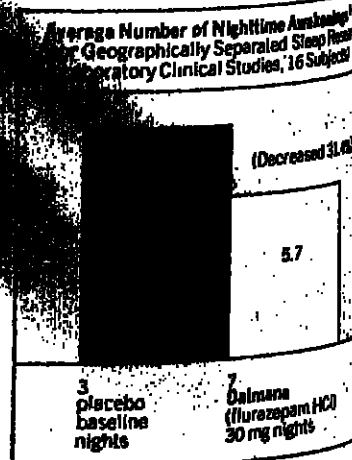
nized individual who has a problem. With all the groups working closely together, we have records and previous visits on which to base a judgment."

The continuity clinic is the pediatric counterpart to the house staff group, he added, but with a somewhat different organization. While the latter has interns, assistant residents, and associate residents working together, the pediatrics group is a horizontal arrangement, with all interns, all first-year residents, and all second-year residents working together, Dr. Glaser said.

He also pointed out that "residents here are actually participating in the practice, and medical students are able to view their work first-hand and form their own judgment. Naturally, we want it to be good so that the most talented physicians of the future are attracted to this kind of patient care."

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- REFERENCES:
1. Karaman I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971.
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 4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ.
 5. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ.

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One Man...and Medicine

ARTHUR M. SACKLER, M.D.
International Publisher, Medical Tribune



Now, A Word From the Opposition

MEDICAL TRIBUNE supports the free exchange of differing views. The following letters are some of the responses to Dr. Sackler's column on the Edelin case, "Doctor, Are You Innocent?" (MT, Mar. 12, 1975).

Your newspaper's coverage of the Edelin conviction is worthy of the 1984 Black is White Literary Award. The "straight" news story by a Special Cor-

respondent sets the tone in the headline—Shock and Dismay—with the predictable bias in the body of the story. Flanking this, we find a "Special Trib-

une Report" by the same author and your sterling piece, "Doctor—Are You Innocent?"

You and your newspaper seem somehow to have missed a basic point. A jury of his peers found Dr. Edelin guilty of manslaughter. He did not kill a fetus—he killed a living human being. Please remove my name at once from your mailing list.

WILLIAM DANIEL DAVIES, M.D.
Evanston, Ill.

I was amazed and disappointed that a fine publication such as MEDICAL TRIBUNE dignified the likes of a Dr. Kenneth C. Edelin with a photo on your front page of the March 12, 1975 issue. Continuation of such published items only aid and abets the act committed.

Certainly there must be other topics

more interesting and deserving to sustain the name of good medicine which is being evaded daily by the very act about which he brags. Let us have no more of this, please. Thank you.

Incidentally, the editorial by Arthur M. Sackler, M.D., was about as enlightening as an overflowing commode.

GERARD A. DEL GRIPPO, M.D.
Lock Haven, Pa.

The vile and vicious anti-Catholic tone of your editorial leads me to make this protest of your appeal to the worst instincts of the society. The kind of abortion performed by Dr. Edelin is disapproved by all segments of the society, all religions, and even a majority of atheists (see Blake, J., *Science*, April 1972).

The tortured non-sequiturs of your argumentation lead me to believe that you were blinded by bigotry in departing from your usual well-reasoned rationale. You find it incomprehensible that a man could be found guilty of manslaughter in "standing by and denying a fetus oxygen and thereby causing its death." Willfully to deny a person oxygen which might have prolonged its life has always been a crime. This is, after all, what the Boston strangler did. Dr. Edelin's true "peers" are said to be his fellow abortionists. Why not have the Godfather judged by his fellow mafioso?

The jury in Boston (whose religion is unknown and irrelevant except to neo-Nazis) have called to issue that notion that every termination of life done under the rubric of "medical procedure" is not to be tolerated by decent Americans.

EUGENE F. DIAMOND, M.D.
Chicago

Regarding Dr. Sackler's editorial on the Edelin case, I am surprised at such verbal frothing-at-the-mouth. Dr. Sackler has always seemed like such a calm, cool, deliberate thinker. It's so unlike him. Does he really mean to compare the culpability of food manufacturers in producing coronary disease (a rather far-fetched and tenuous theory at best) with the deliberate actions and inactions of Dr. Edelin? Dr. Edelin, in essence, delivered a premature baby by C-section, and then deliberately neglected it to death, by his own admission.

As Dr. Sackler suggests, Dr. Edelin's conviction will probably be overturned—because of technical flaws in his trial—but not because his actions, *per se*, were so noble. He may or may not be guilty of manslaughter, but on the other hand, it ill-behoves so many physicians to make a hero of him, or to publicly applaud his second-trimester "abortion" activities as a prototype of conduct which all physicians should emulate.

Such an attitude is unlikely to redound to our credit in the future.

Out of embarrassment for Dr. Sackler, I will merely pass over his not-too-subtle appeal to religious bigotry, without further elaboration.

As for emotionalism, it surely looks like the shoe is on the other foot this time.

JAMES H. FORD, M.D.
Lynwood, Calif.

We know Librium works. (chlordiazepoxide HCl)

We're still learning more about how and why.

Value of continuing animal research

Clinical knowledge of Librium is extensive, yet its mode of action remains under continuing study. Data from animal experiments have been presented here for their intrinsic interest and because such findings often provide direction to new research, both experimental and clinical. However, conclusions from such studies may not always be extrapolated to humans.

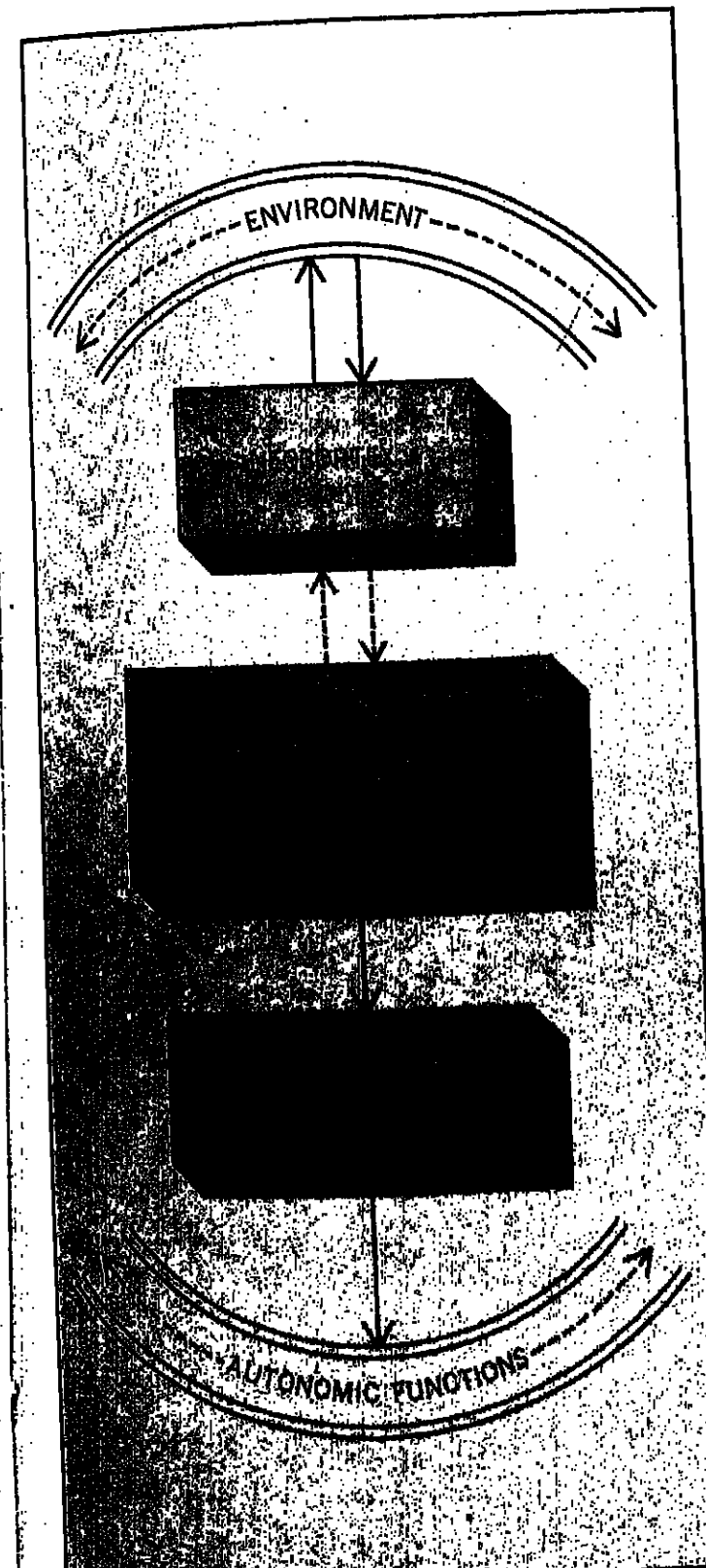
Is the limbic system the "Librium (chlordiazepoxide HCl) system"?

A great deal of experimentation on various animal species suggests that the limbic system is the principal site of action of Librium. Thus, in freely moving cats with electrodes implanted in the brain, Librium 5 mg/kg i.p. slowed electrical activity in the hippocampus, amygdala and septal areas but not in the neocortex which was significantly affected only at higher doses.^{1,2} Current investigations on monkeys,^{3,4} however, indicate that other subcortical structures may be implicated in the effect of Librium.

Other investigators, through electrophysiologic studies⁵ in intact, conscious cats and monkeys, have demonstrated that chlordiazepoxide activates structures involved in the rewarding system—the preoptic area, lateral hypothalamus, septal region and hippocampal formation. At the same time, it appears to inhibit structures implicated in aversive behavior—the thalamic nuclei of the diencephalon and the midbrain reticular formation (MRF).

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Schema demonstrating hypothetical pathways of emotional activity and its related expression in laboratory animals.

Clinical significance of excessive anxiety

Anxiety, when inappropriate and immoderate, may not only have adverse psychological effects but may also cause various somatic disturbances. Reduction of excessive anxiety thus contributes to relief of anxiety-linked emotional and physical disorders.

Antianxiety action of Librium (chlordiazepoxide HCl)

The dependable action of Librium has been demonstrated in the relief of excessive anxiety and tension occurring alone or in association with functional and organic disorders—usually without adversely affecting performance. Librium is often used concomitantly, when anxiety is a contributing or complicating factor, with certain specific medications of other classes of drugs, e.g., cardiac glycosides, diuretics and antihypertensives.

Adjunctive use of Librium is recommended when counseling, reassurance or other nonpharmacologic measures alone are not considered sufficiently effective. When anxiety has been reduced to manageable levels, therapy with Librium should be discontinued.

Librium®
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5 mg, 10 mg, 25 mg capsules



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to make it more useful to you.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other

CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage without withdrawal symptoms (including convulsions).

following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards. **Precautions:** In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation,

increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Para-

doxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and

oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin

eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making

periodic blood counts and liver function tests advisable during protracted therapy. **Supplied:** Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.



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wine talk

By JOHN CHAMBERS
Author and Consultant to
Morrell & Company,
New York Wine Merchants

Aging Wine

Dr. ARTHUR BIEGANOWSKI of New York is one of the most ardent wine enthusiasts of my acquaintance. Indeed, at his home it would be almost an insult to ask for Scotch. He has a genius for coming up with surprises, and his latest was a master stroke. Somehow he had managed to find a bottle of ruby port that had lain in a cellar over 30 years. To taste the delicacy and beauty of this comparatively inexpensive, generally available wine, given 30 years' aging, was a potent reminder of what age can do for a wine with the capacity to respond to it.

Some wines do not need aging and are best drunk very young. These are light wines—rosés and whites for the most part, and a few of the lightest reds like Beaujolais, Bardolino, or inexpensive Chianti. Only the better white Burgundies and Graves, the Pinot Chardonnays of California, Barsacs and Sauternes, the white Rhones, and the spittles, austeres, and up of Germany need more than a year or two in the bottle, and of these, only the white Rhones, Barsacs, Sauternes, and sweeter German wines can be kept with impunity beyond seven years.

With red wines the problem of aging becomes more complicated. Here it is not only a question of a particular wine, but also the character of a vintage. For example, most of the 1967 red Bordeaux are ready for present drinking, whereas the bigger 1966's are a year or two away. The best rule of thumb is that red Bordeaux from the Médoc require seven years, from St. Emilion and Pomerol six years, and from elsewhere in Bordeaux four years. If the vintage is listed as a "long-lived" one, add a year or two.

Burgundy Needs Less Time

Red Burgundy is ready sooner. Wines from the Côte de Nuits require six years in a big vintage, whereas most Côte de Beaune are ready in four years. Only the biggest Beaujolais will improve beyond three years. In the Rhone valley the biggest wines require seven years of bottle age in most vintages, but Côtes du Rhone (one of the better buys on the market) need only two to three years. The same holds true of the Loire reds and of the so-called country reds from elsewhere in France.

In Italy, Spain, and Portugal, price is a fair guide to aging requirements. The more expensive wines need six to seven years in the bottle, while two to three years is sufficient for the less expensive. The other red wines of Europe can generally be drunk when marketed.

Most reds from North and South America can also be drunk when purchased, the major exceptions being the better California Cabernet Sauvignons, Petite Sirahs, and Zinfandels, all of which benefit from additional bottle age.

Next Month: Research and Viticulture

Strike Pact Terms May Have Wide Impact

Continued from page 1
hospital, consisting of an equal number of members from staff and administration, and charged with formulating "appropriate work schedules" and hearing grievances. Salaries, which now range from \$13,500 for an intern to \$19,200 for a 6th year resident (PGY 7) will rise 8 per cent, with an across-the-board cost of living sum of \$250 added.

Broad Impact Foreseen

Dr. Robert G. Harmon, president of the Physicians National Housestaff Association, which supported the strike, told MEDICAL TRIBUNE that he thought the point would not be lost on "exploitative" hospital administrators and senior staff everywhere.

"It's a major victory, and it's going to give momentum to National Labor Relations Board negotiations for reasonable hours and working conditions in many hospitals—for example, Los Angeles County Hospital and the District of Columbia Children's Hospital," Dr. Harmon said. He noted that Dr. Malcolm C. Todd, president of the A.M.A., had given his blessing to the strike, a move that surprised some and could not help enhancing the possibility of similar changes, if not strikes, elsewhere.

Dr. Todd's statement said in part that "in important respects, this is a strike for better patient care... When a physician has to work 50 hours straight or 100 hours in a week, it is not only tough on him or her, it is also a threat to the quality of care the patient is receiving."

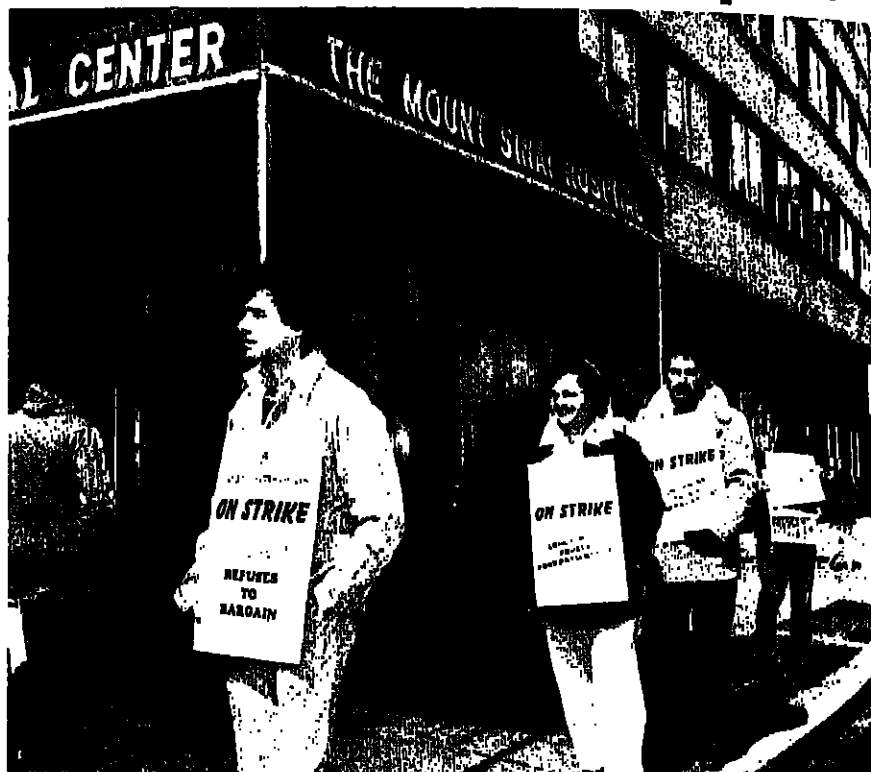
Hospitals Reject Implications

A spokesman for the A.M.A. told MEDICAL TRIBUNE that although the Association expected criticism from its membership concerning the Todd statement, little had yet been received. However, officials of the struck hospitals in New York vigorously rejected the implications of the statement, saying that the League of Voluntary Hospitals included some of the finest medical facilities in the world and would never do anything that threatens patient care.



Delegates of Committee of Interns and Residents take a straw vote on contract offer by the League of Voluntary Hospitals during negotiations.

C.I.R. Photo



In the first doctors' strike recorded in the U.S., picket lines surrounded some of the most prestigious hospitals in the country, including Mount Sinai, above.

Dr. S. David Pomrinse, director of Mount Sinai Hospital, one of those affected, asserted that long hours are necessary for house officers' training and are not detrimental to interns' and residents' health or to the care they give their patients. He maintained that even on the longest shifts, staffers have time for naps in between cases.

"Our chiefs of service are just as concerned as they are about their health," he said of the interns and residents. "There is adequate time for rest." Until recent years, he said, schedules were even tougher, with house officers being on duty three days and two nights on a regular basis.

Jess Solivan, president of the League, backed Dr. Pomrinse. Regardless of scheduling, he said, "It's expected that when a doctor reaches the point where he's not able to produce or to avail himself of the learning process, he'll say, 'Hey, give me some relief!'"

This just isn't so, contended Dr. Mark Fleischer, a medical intern on the picket line at Brookdale Hospital Medical Center in Brooklyn. "What

are you going to do at 3:00 A.M.? Call your buddy, who's in the same condition you are and say, 'Hey, give me some relief!'"

An attending physician at one of the struck hospitals confirmed Dr. Fleischer's statements. This physician, who wished to remain anonymous, recalled that when he took his internship at Montefiore Hospital and Medical Center in the Bronx, which was also affected by the strike, some few interns did call for help from their chiefs of service.

Retaliation Recalled

"In most cases they got it," he related. "But they always paid for it later. They were branded as weak sisters who couldn't take the strain of being a doctor, and in some cases I know of, they weren't asked back to take their residencies at Montefiore the following year."

And Dr. Don Rubin, a medical intern at Mount Sinai, pointed out that a house officer on a 36- to 48-hour tour

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of duty may actually get less sleep than Dr. Pomrinse did on his 60-hour shifts. "Medicine has become much more complex in recent years," said Dr. Rubin, who took his turn on the picket line at his institution. "There's much more that we can do for patients." "For instance, when a patient went into cardiac arrest in Dr. Pomrinse's time, the intern signed the death certificate and went back to bed. Today, he's going to be working with the cardiac emergency team for at least two hours, saving the patient's life." "And it's the same with peritoneal dialysis, which they didn't have until the early 1960s. If a patient needs dialysis today, he doesn't die. But I'm sitting up all night with him."

Out-of-Title Work Cited

Dr. Rubin tied the demand for shorter hours to the out-of-title work issue. "A lot of what I do, especially at night, isn't doctor work. Watching that dialysis patient should be done by a nurse, with me on call. And I spend a lot of time wheeling patients around in the hospital or delivering bloods to the lab."

Not all the house officers at League hospitals went out on strike. At Brookdale, for instance, many of the senior medical residents stayed on, while most of their junior colleagues walked the picket line.

"Some of us were angry about that," Dr. Fleischer said. "But in a way, it made things easier on me to know there were doctors in there taking care of the patients."

Most of the striking house officers felt as Dr. Fleischer did, and at many of the struck institutions the house officers made arrangements with the hospital to provide emergency patient care.

"It wasn't unusual" a surgery resident at one such facility said, "to see a picket put down his sign, go into the emergency room to help out with a renal crisis, and then come back out and re-



Left, a surprised Dr. Anthony Bottone, C.I.R. delegate, holds aloft news of A.M.A. support. Above left, delegates found negotiating almost as tiring as duty schedules they sought to change. Above right, Dr. Diane Chen-Cohen, Long Island Jewish-Hillside Medical Center delegate, checks in while colleague catnaps.

MEDICAL TRIBUNE

19

Tribune Economic Analysis



Company Notes In Place of Pay Cuts Suggested

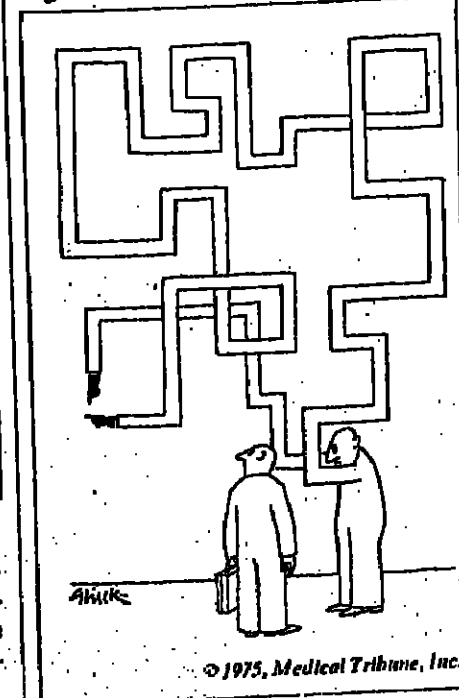
The very magnitude of today's debt burden offers a handle for avoiding a repeat performance of the 1930s' depression that is clearly threatening. Over-indebtedness is the specific abuse responsible for hyper-inflation. Booms invite an overload of debt, which accentuates busts.

The sound way to undo today's damage, and to avoid still more, is to lighten the debt load by trading on the troublesome fact that people on payrolls are struggling with every bit as cruel a debt overload as outfits to meet payrolls. The banks are at least as anxious over the consequences of their over-lending as their debtors are over the consequences of their over-borrowing.

A 3-Way Compromise

The wobbling companies, their anxious banks, and the petrified people on their payrolls would all be ahead if they worked a three-way compromise. Assume that the management in trouble could show both the banks on its back and the people on its payroll how much difference a reasonable cut would make. And that management demonstrated its good faith by practicing austerity on expense accounts and taking an appropriate cut itself. All three partners in the debt squeeze would be ahead if management "borrowed" the pay cut from labor instead of just taking it.

Issuing company notes to everyone on the payroll in order to cover the cut agreed upon would kill three birds with one stone. Management would cut costs. People now worrying that each paycheck might be the last would get a new asset with a fighting chance to keep the money coming. The banks would wind up with a better-fixed business borrower, plus a whole new group of family circle customers for the consumer installment loans they are pushing so hard.



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A patient often benefits by a greater understanding of his treatment program. You may find it helpful to make your patient aware that the purpose of therapy with Valium is to help reduce discomforting and disabling symptoms of excessive psychic tension and anxiety. It is beneficial for him to understand that much of his tension and anxiety can be relieved by your reassurance and counseling, and that these measures can do more than anything else to help him cope with his basic problems. The patient is reassured in knowing he can expect his medication to help him avoid feeling overwhelmed by his symptoms.

And it's also good for him to realize that he will be taking Valium only as long as he needs it.

Your expressed confidence in the medication prescribed, and the positive atmosphere in which therapy is given and accepted, work to the patient's advantage.

Selection of a dosage regimen is an important consideration when Valium (diazepam) is prescribed, and dosage should be individualized to achieve maximum beneficial effect. If the patient understands clearly when and how much to take, and if he knows why it's to his benefit to follow the regimen closely, the chances are better that he will take the medication precisely as directed. That should help avoid missed doses and discourage taking too much or too little medication — all of which can have an undesirable effect on the management of the patient's condition.

*"It's important that you
follow my directions
closely."*

*"I'll see you again the week
after next and we'll see
how you're making out."*

Your patient is often likely to feel reassured when you talk about seeing him again to check his progress. A planned visit evidences your continued interest and affords the patient an opportunity to report improvement he has made and to relate whatever continuing or additional difficulties he may be experiencing. It's also a chance for him to describe his response to therapy with Valium.

During follow-up visits, as your patient talks about his medication and about its effects on his symptoms, he will provide the kind of information that will be of great help in evaluating total therapy, adjusting the dosage of Valium, or discontinuing the medication entirely if that seems indicated.

Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets
for individualized treatment of psychic tension

ROCHE

Please see the following page for a summary of product information.



Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets

Prompt, effective action. Valium (diazepam) works rapidly to relieve pronounced psychic tension in patients overreacting to stress and in psychoneurotic patients.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other anti-

depressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Dosage flexibility. Scored Valium 2-, 5-, and 10-mg tablets give you dosage flexibility no tranquilizer capsule can match.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-B-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.

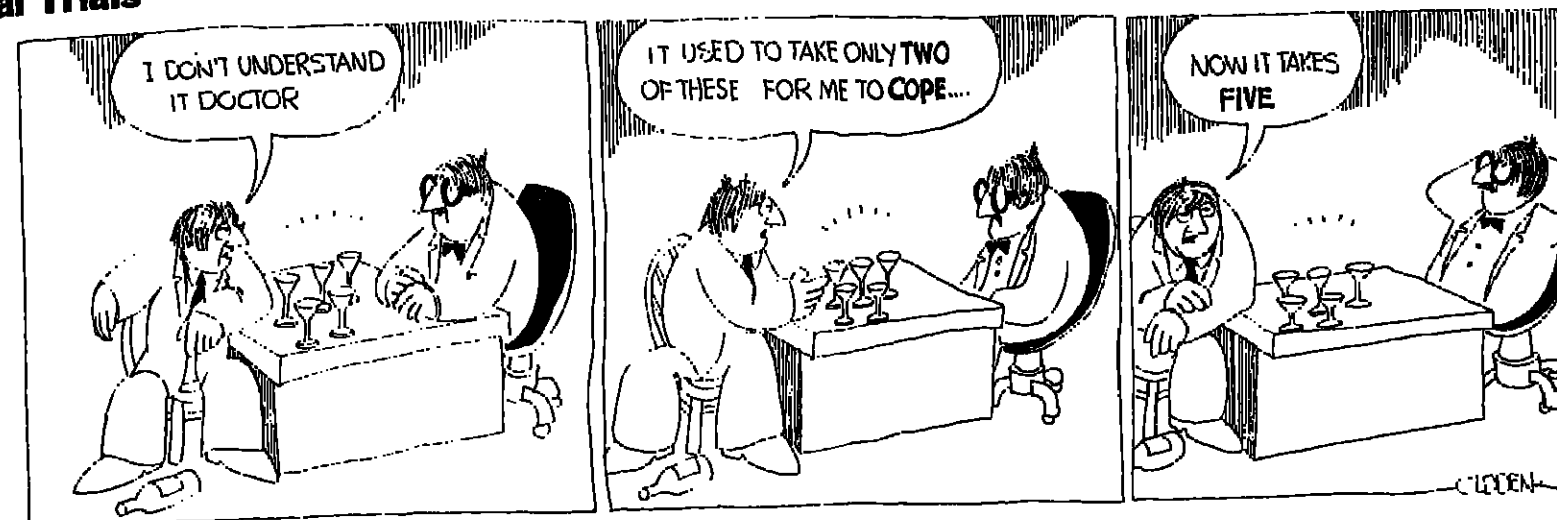


Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

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MEDICAL TRIBUNE

Clinical Trials



TRIBUNE SPORTS REPORT

Hang Gliding Said to Point Up Need for 'Action Priorities'

Medical Tribune Report

SAN FRANCISCO—Dr. Arthur E. Ellison of Williamstown, Mass., cited the fast-growing sport of hang gliding as an example of the need to establish "action priorities" in athletic medicine through coordination of research efforts.

He told a meeting of the American Orthopaedic Society for Sports Medicine here that participants in this dangerous pastime have increased from 200 to 11,000 since 1972, with gliding kites now being sold at a rate of about 1,000 a month.

A Death a Month in California

While the exact injury rate is not known, he said, Rancho Los Amigos in Los Angeles has six paraplegic patients who are victims of hang gliding accidents, and California alone averages one fatality a month from this sport.

Most of the injuries are to the extremities, he said.

As some of the factors in the accidents, Dr. Ellison cited the weather,

the terrain, pilot error, and kite failure.

A thorough survey, he said, might suggest that a special action program is required, including: modification of equipment to provide such safety devices as a parachute or an ejection suit; special padding, helmets, gloves, or boots; elimination of flying over dangerous terrain; licensing; a ban on unsound kites; or, if the toll is found to be too high, outlawing of hang gliding altogether.



Calif. Acupuncture Unit With Few MDs Likely

Continued from page 9

puncture which is lobbying to change the Moscone bill.

"There is room for traditional acupuncturists," Dr. Wong said in an interview with MEDICAL TRIBUNE, "but they should be required to show expertise in basic science. By the same token, we also think that M.D.s should not be given carte blanche, but ought to be required to take 100 to 150 hours of acupuncture training, as they must do now in New York."

Alternative Makeup Proposed

"As for the makeup of the Advisory Board, our alternative suggestion is a 10-member Board with the following distribution: one member from the State Board of Medical Examiners; four physician-acupuncturists; one dentist-acupuncturist; one non-medical, academic, research-oriented Ph.D. with at least five years experience with acupuncture; and three traditional acupuncturists trained in Japan, China, or Korea, with at least ten years experience, and demonstrated knowledge of western concepts of anatomy, physiology, etc."

"Our main motive," he added, "is to see that the public is fully protected,

and acupuncture doesn't go 'down the pipes' as quackery."

Sources in Gov. Brown's office told MEDICAL TRIBUNE that he is waiting to study the final version of the Moscone bill before deciding whether to sign it; they said the Assembly often amends or adds to bills received from the Senate.

Neighboring Nevada, in 1973, was the first state to legalize the practice of acupuncture by non-physicians without medical supervision. In the rest of the country, there is a patchwork of regulations, often stipulating that acupunc-

ture can only be performed by M.D.'s for research purposes.

The A.M.A. has not adopted an official policy on acupuncture. However, the August, 1974 statement issued by an A.M.A. delegation on its return from the Peoples' Republic of China, said that "acupuncture analgesia merits controlled experimental study," while warning that "acupuncture therapy should be regarded as the practice of medicine in an experimental phase, permissible only in qualified investigational settings."

Gonorrhea in Women Declared to Be Often Symptomatic

Medical Tribune World Service

GENEVA—Gonorrhea in women cannot be regarded as commonly nonsymptomatic, a United States physician stated here at a World Health Organization-sponsored meeting on health education in the control of sexually transmitted diseases.

Estimates that up to 60 per cent of infected women, and 10-20 per cent of men, are without symptoms, are largely based on the experience of physicians working in VD clinics, said Dr. King K. Holmes, of University of Washington, Seattle.

Such views, he said, are not corrected by probability sampling, case control, or cohort studies, or from the syndrome-oriented experience of certain subspecialties, such as rheumatology and gynecology.

Acute Symptoms in 80 %

"About 80 per cent of women seen in the University of Washington specialty clinics and emergency room have sought treatment because of acute symptoms," Dr. Holmes said.

As manifestations in women that are suggestive of, or compatible with, gon-

orrhea, he cited lower abdominal pain, abnormal vaginal discharge, dysuria and urinary frequency, rectal symptoms, joint pains, and skin lesions, and probably abnormal menstrual bleeding also.

While, currently, 10 to 20 per cent of male patients at VD clinics have no symptoms, this figure also bears no relationship to the true proportion of new cases of this kind, Dr. Holmes asserted.

"In an unpublished cohort study, we have found this proportion to be only 3 per cent," he reported.

by G.

IMMATERIA MEDICA

Minnesota Medicine's Mascot

The new editor-in-chief of Minnesota Medicine, Dr. Richard L. Reece, has introduced a mascot into his columns. Why? "Because I have one in mind, that's why," says Editor Reeves. "His name is minny."

That brought us up short. Unisex, we figured, for Minnesota. Editor Reeves says minny is "a literary cockroach who composes free verse by hurling himself head downward against the typewriter keys..."

Like Don Marquis' archbald, of archbald and mehtabel fame, from whom minny is descended, he can't manage capital letters or punctuation on the typewriter. "minny is bold, disrespectful, fun-loving, contemptuous of detail, and hungry for the literary life," says Editor Reeves, who in his March issue published minny's first poem:

my minnesota medicine editor
I accept the position
because mascots bring luck
and you will need plenty

Long live minny the mascot of Minnesota Medicine! Who knows? This mascot business may be as contagious as measles. We could have ginny for Virginia Med. M., flo for J. Florida M.A., pa for Pennsylvania Med., tex for Texas M., mo for Missouri Med., and missy for J. Mississippi Med. Ass.

But now that they are teaching chimps to talk and typewrite, nobody says all mascots have to be cockroaches. In fact, we know some who are just cute nurses.